Submitted to
The Tamil Nadu Dr.M.G.R.Medical University

FOR

M.D.DEGREE EXAMINATION

BRANCH – 1 (GENERAL MEDICINE)

THE TAMIL NADU DR.M.G.R.MEDICAL UNIVERSITY

CHENNAI, INDIA

MARCH 2008

CERTIFICATE

This is to certify that this dissertation entitled **"A Study on Electrocardiographic and Echocardiographic Changes in Chronic Kidney Disease"** is bonafide work done by **Dr.Sangeetha.V,** postgraduate student, Department of Internal Medicine, Government Kilpauk Medical College, Chennai-10 under my direct guidance and supervision in fulfillment of regulation of the Tamil Nadu Dr.M.G.R. Medical University for the award of M.D. Degree, Branch I, part II (General Medicine) during the academic period from may 2005 to march 2008.

Prof.Dr.M. Dhanapal, M.D.D.M (Cardio)
The Dean
Govt. Kilpauk Medical College,
Chennai-600 010

Prof. Dr. N.Gunasekaran, M.D.D.T.C.D,
Professor of Internal Medicine,
Govt. Kilpauk Medical College,
Chennai – 600 010

Prof.Dr.G.Rajendran, M.D,
Professor & Head of the Dept,
Dept. of Internal Medicine,
Govt. Kilpauk Medical College,
Chennai – 600 010

ACKNOWLEDGEMENT

I am very much thankful to the Dean **Prof.M.Dhanapal, M.D.D.M (Cardio),** Govt. Kilpauk Medical College, Chennai & the Superintendent, **Prof.R.N.M.Francis,M.S,** Govt. Royapettah Hospital for granting me permission to utilize the facilities of the hospital for the study.

I am deeply indebted to my respected and beloved teacher **Prof.N.Gunasekaran.M.D.D.T.C.D,** Professor of medicine, Govt. Kilpauk Medical College for encouraging and extending invaluable guidance to perform and complete this dissertation. I owe a deep sense of gratitude to **Prof.Joseph Navaseelan, M.D**., Professor of Medicine, Govt. Kilpauk Medical College for his support and teachings.

I express my profound thanks to **Prof.G.Rajendran.M.D,** Professor and Head of the Department of Internal Medicine, Govt. Kilpauk Medical College for being a constant source of inspiration and guidance.

I thank **Prof.J.H.Balasingh.M.D.D.M(Nephro)**, Professor of Nephrology, Govt. Kilpauk Medical College and **Prof.Narayananasamy Senguttuvan.M.D.D.M(Cardio)** professor of cardiology, Govt. Kilpauk Medical College for their encouragement and support during the study.

I wish to thank **Dr.P.Parandhaman.M.D.D.T.C.D, Dr.G.Ranjani.M.D and Dr.S.Kalaichelvi.M.D.D.G.O,** Assistant Professors, Department of Medicine, Kilpauk Medical College for their valuable suggestions.

I also express my gratitude to **Dr.Surendran.M.D, Dr.Jayaprakash.M.D, Dr.G.Sundaramurthy.M.D, Dr.Manickam,M.D,** Assistant Professors, Department of Cardiology, Govt. Kilpauk Medical College and **Dr.J.Vijula,M.D, Dr.Dinesh,M.D,** Assistant Professors, Department of Nephrology, Govt. Kilpauk Medical College for their valuable guidance.

I thank all my fellow postgraduate students, house surgeons and the staff of our college for their contribution to the study.

Last but not the least, I would like to express my heartfelt gratitude to all our patients, but for whose co-operation, the study would not have been successful.

CONTENTS

AIM OF THE STUDY

1. To evaluate the biochemical, radiological and ultrasonographic aspects of Chronic Kidney Disease at the time of diagnosis.

2. To study the prevalence of cardiac changes in patients with Chronic Kidney Disease(CKD)

3. To study the Left Ventricular function, and its relationship with duration, symptomatology and blood bio-chemistry (severity) in patients with CKD.

INTRODUCTION

In health, the volume and composition of body fluids vary within narrow limits and kidneys are largely responsible for maintaining this state. They also subserve a host of metabolic and endocrine functions. The failure of renal function results ultimately in alterations of milieu interior, that affects every organ system in the body.

Chronic Kidney Disease is a clinical syndrome due to persistent renal dysfunction leading to excretory, metabolic and synthetic failure culminating in accumulation of non protein nitrogenous substances and presents with varied clinical features. As soon as the cause for CKD is established, further evaluation is used as needed to preserve or restore glomerular filtration rate. In particular, evaluation of cardiovascular risk factors is critical, because of high rate of cardiovascular complications in CKD.

History and measurement of renal size are helpful in establishing the chronicity of disease[1]. It is important to note that no specific blood or urine test unequivocally differentiates acute from chronic kidney disease. Creatinine concentration in finger nail can establish chronicity but determination is not available in clinical practice[2]. The most sensitive and specific test for establishing the chronicity of kidney disease is measurement of renal size. Currently renal ultrasonography is the technique of choice.

The finding of small kidneys (i.e. small, relative to body size) on renal ultrasonography is a reliable indicator of CKD. Renal biopsy is the most definitive method of differentiating acute from chronic kidney disease.

Easy fatigability, dyspnoea, pedal edema, syncope, angina are the usual cardiovascular symptoms that are frequently encountered in patients with advanced renal failure. Structural and functional cardiovascular evaluation is done using X-Rays, Electrocardiography, and Echocardiography.

Cardiovascular disease accounts for about 50% of all deaths in patients with CKD. Left Ventricular dysfunction is estimated to be present in 65% of such patients. All patients with mild to moderate Left Ventricular systolic dysfunction had normalization of heart function with renal replacement therapy.

REVIEW OF LITERATURE

1. CKD – Historical aspects
2. Definition & Staging of CKD
3. Pathophysiology of Uremia and clinical features
4. Cardiovascular Manifestations in CKD
5. Electrocardiographic changes in CKD
6. Echocardiography

Before going for discussion about cardiac manifestations in CKD a short description about CKD will be useful.

CKD – Historical aspects

The term Uremia was coined by Piorry and L'Heretier in 1840, because they thought that the clinical manifestations of kidney diseases was due to retention of urea in the blood. This theory persisted up to twentieth century and the role of urea and other related toxins were particularly emphasized.

The modern era of uremic symptoms began in the first half of twentyfirst century with works of Richard Bright. He described the progression of symptoms in patients suffering from kidney diseases which later came to be called as Bright's disease.

Definition of CKD

CKD is defined as kidney damage with or without decreased glomerular filtration rate (GFR), manifested as either pathologic abnormalities, or markers of kidney damage that include abnormalities in composition of blood or urine, abnormal renal imaging findings and GFR less than 60ml/min 1.73m^2. This broad definition includes patients with or without symptoms of kidney diseases.

Staging of CKD

K/DOQI Guidelines

Stage	Description	Estimated GFR In ml / min
	At increased risk	> 90
1.	Kidney damaged with Normal or increased GFR	≥ 90
2.	Kidney damaged with mildly Decreased GFR	60-89
3.	Moderately decreased GFR	30-59
4.	Severely decreased GFR	15-29

5.	Kidney failure	< 15

Pathophysiology of Uremia

In Chronic Renal Failure (CRF) compensatory and adaptive mechanisms maintain acceptable health until the GFR is about 10-15ml/min and life sustaining renal excretory and homeostatic functions continue until the GFR is less than 5ml/min. The favored explanation centers on “intact nephron hypothesis” first proposed by Bricker, which states that the functioning nephrons compensate for their non-functioning nephrons. This does not come without the price and “trade off hypothesis” has to be considered along side the intact nephron hypothesis. The best example is the secondary hyperparathyroidism to maintain the normal phosphate level which in turn leads to metastatic calcification.

Although many of the manifestations of uremic syndrome are attributed to derangement in electrolyte concentrations, fluid imbalance and endocrine deficiencies, there are others that are explained by action of substances and metabolites retained because of excretory failure. Examples include encephalopathy, platelet dysfunction, glucose intolerance, and anemia and leukocyte dysfunction. The substances those are responsible for this uremic syndrome are called as Middle Molecules.

Some of the Examples are:

1. Homocysteine – Atherogenic
2. Methyl guanidine – neurotoxin that causes peripheral neuropathy
3. Amino guanidine – potent inhibitor of Nitric Oxide that leads to hypertension
4. β2 Micro globulin – amyloid
5. Drugs such as Morphine – accumulate and cause encephalopathy.

Cardiovascular Manifestations in CKD

Introduction

Cardiovascular disease is recognized as the predominant cause of death in CKD. Most clinical consequences of cardiac disease result from cardiomyopathy or ischemic heart disease. Cardiomyopathy may manifest as an enlarged, dilated Left Ventricle, with systolic dysfunction or hypertrophic ventricle with diastolic dysfunction, with or without myocardial ischemia. CKD causes accelerated atherosclerosis and also arteriosclerosis. Ischemic symptoms result from Coronary Artery Disease (CAD) or arteriosclerosis. Arteriosclerosis contribute directly to ischemic symptoms, Left Ventricular hypertrophy (LVH), systolic

dysfunction by increasing cardiac workload. CAD predisposes to diastolic dysfunction (DD) and systolic dysfunction.

Most valvular lesions observed in patients with CKD are acquired and develop from dystrophic calcifications of valvular annulus and leaflets, particularly aortic and mitral valves[4]. Such calcification is present in 55% of aortic valve and 39% of mitral valve[5, 6]. Once considered benign, aortic valve sclerosis is associated with increased cardiovascular mortality in general community[7]. LVH is evident in 40% of the patients with moderate renal insufficiency[8] and 75% of those commencing dialysis[9]. Associated risk factors including Diabetes, Hypertension, tobacco use and anemia predisposed to much more rapid development of symptomatic cardiomyopathy[10].

Risk factors for cardiovascular involvement in CKD

1. Hypertension

It is prominent in all stages of CKD whatever the etiology. It is a strong predictor for LVH, cardiac dilatation, cardiac failure, ischemic heart disease and worsening of atherosclerosis[38]. There is a blunting of the nocturnal dip in blood pressure in uremia which puts the patients at higher risk for vascular diseases. Impairment of cardiac perfusion during

diastole, particularly in the presence of LVH or decreased aortic compliance leads to ischemic myocardial damage.

2. Lipids

Renal dyslipidemia[39, 40] is reflected in an abnormal apolipoprotein profile – decreased High Density Lipoprotein and increased concentration of Very Low Density Lipoprotein, Intermediate Density Lipoprotein and Low Density Lipoprotein. A significantly decreased Apo A-II to Apo C-III is the hallmark of altered lipoprotein composition in renal disease, thereby promoting atherosclerosis.

3. Diabetes

It predicts deterioration in cardiovascular state, regardless of the presence of cardiovascular disease at baseline[41]. Diabetes leads to microalbuminuria, a marker of early diabetic nephropathy, that signifies vascular endothelial dysfunction. Echocardiographic LVH is probably a more frequent finding in hypertensive diabetic patients than in hypertensive non-diabetic patients.

4. Hypoalbuminemia

It is emerging as a powerful risk factor for cardiovascular mortality besides all cause mortality, especially in dialysis patients. Malnutrition

also can lead to low folate, B12 levels and low arginine in turn leading further to hyperhomocysteinemia and impaired Nitric oxide synthesis. Low level of antithrombotic proteins leads to hypercoagulability[54]. Inflammation also causes decrease in albumin synthesis and increase in albumin fractional catabolic rate. This inflammatory response alters the endothelium and plasma protein composition in ways favoring vascular injury.

5.Malnutrition-Inflammation-Atherosclerosis Syndrome(MIA)

Uremia is a state of chronic inflammation. Reduced renal clearance of cytokines, accumulation of Advanced Glycation End Products (AGE) and unrecognized persistent infections are some of the causes. Levels of pro inflammatory cytokines such as IL_1, IL_6, TNF α are increased 8 to 10 fold. IL_6 is an important pro atherogenic cytokine that alter insulin sensitivity and endothelial function. It is a strong stimulant of adhesion molecules (VCAM, ICAM) which mediates attachment and migration of leucocytes across the endothelial surface. The sustained inflammatory reaction promotes endothelial dysfunction, oxidative stress, complement activation and leads to increased cardiovascular mortality.

6. Hyperhomocysteinemia

It is a strong predictor of cardiovascular disease in the general population[55,56] and appears to be associated with further risk in patients with CKD[57]. In CRF, homocysteine levels range from moderate (16-30µmol/L) to intermediate (30-100µmol/L). It enhances vascular smooth muscle proliferation, increases platelet aggregation and act on the coagulation cascade and fibrinolysis directly inducing a prothrombotic environment or by acting in a synergistic manner with other risk factors. It activates coagulation factors V, X, XII along with decreased activation of protein C and cell surface thrombomodulin and modulation of tissue plasminogen activator binding to its endothelial receptor -annexin II.

The proposed mechanisms of homocysteine toxicity are oxidative stress through production of reactive oxygen species, binding to nitric oxide, production of homocysteinylated /acylated proteins and accumulation of its precursor S-Adenosyl homocysteine-a potent inhibitor of transmethylation reactions.

7. Role of ADMA(Asymmetric Dimethyl Arginine)

ADMA is a new emerging cardiovascular risk factor considered in uremic patients. It is a competitive Nitric Oxide synthetase inhibitor

leading to decreased Nitrous Oxide availability. ADMA is degraded by dimethyl arginine dimethyl aminohydrolase-an enzyme rich in renal tissue. With advancing renal failure and loss of renal mass ADMA accumulates. In ESRD, it is the second strongest predictor of cardiovascular mortality, after age, among the traditional risk factors.

8. Angiotensin II

The Renin Angiotensin system is activated in most of the renal diseases especially in diabetics and hypertensive. Emerging evidences suggest that the resultant increased Angiotensin II is not only a vasoactive peptide but also a true cytokine that regulates cell growth, inflammation and fibrosis. Angiotensin-II increases TNF α production which regulates various cell processes including cell proliferation and production of other cytokines and adhesion molecules. It also up regulates other pro-inflammatory mediators-IL-6, NF-k β and thus plays an active role on the inflammatory response in renal diseases. It stimulates superoxide lipid per oxidation and inactivation of NO producing oxidative stress.

Atherosclerosis is promoted by Angiotensin-II, by production of lipid into the foam cells of the vessel wall, and by Endothelial Dysfunction. It induces endothelial cell apoptosis, which has dramatic effects on the platelet cell binding and on the inflammatory process. The various

metalloproteinases induced by Ang-II,MMP-1, MMP-9, etc. lead to proliferation, migration and hypertrophy of vascular smooth muscles and promote matrix expansion and fibrosis.

9. Calcium, Phosphorus and Parathormone (PTH) in CKD

Progressive nephron loss is associated with phosphate retention and hypocalcemia. This triggers increased parathormone activity. The secondary hyperparathyroidism along with hyperphosphatemia and increased calcium phosphate ion product are identified as independent cardiovascular risk factors. Decreased cardiac contraction, LVH and valvular calcification culminate. An increase in calcium-phosphorous product > 60 mg^2/dl^2 promotes metastatic calcification. Vascular calcification begins 10-20 years earlier than in the general population.

There is substantial experimental and clinical evidence that the hyperparathyroid state and altered vitamin D status found in uremia contribute to cardiomyopathy, LV hypertrophy, LV fibrosis, atherosclerosis, myocardial ischemia, and vascular and cardiac calcification[61].

A viable hypothesis is that the disturbed divalent ion metabolism promotes vascular calcification, which produces non-compliant major

vessels. This in turn predisposes to LV hypertrophy, cardiac disease, and subsequent death.

10. **Oxidative Stress**

Oxidative stress is said to occur when there is an imbalance between formation of reactive oxygen species (ROS) and antioxidant defense mechanisms. ROS (e.g. hydrogen peroxide, free radicals such as superoxide, hydroxyl radical) are continuously formed in vivo and play an important role in host defense against tumor cells and pathogens. A number of enzymatic and non enzymatic defense mechanisms have evolved to "detoxify" ROS. The predominant non enzymatic agents include vitamin E, vitamin C, selenium, and zinc. Superoxide dismutase and glutathione peroxidase are the main antioxidants. It is thought that oxidative stress is important in the formation of atheroma, because it generates lipid peroxidation products that are consistently found in atheromatous streaks and sclerotic lesions[59, 60].

Compelling evidence indicates that oxidative stress is an important trigger in the complex chain of events leading to atherosclerosis in CKD. Enhanced oxidative stress may be identified by an increase in the products of lipid per oxidation (e.g. malondialdehyde), a decrease in substances that enhance oxidative resistance (e.g. plasmalogen), or a

decrease in reducing substances (e.g. glutathione). There is evidence for all of these in CKD.

11. Increased extra cellular Volume

At all stages of CKD, sodium and water overload may cause plasma volume expansion, LV dilatation and LV hypertrophy. However, the main group affected is the dialysis patients. LV hypertrophy is more severe in long-term peritoneal dialysis patients than in hemodialysis patients[46]. This finding is associated with evidence of more pronounced volume expansion, hypertension, and hypoalbuminemia.

12. Arteriovenous Fistulas

Blood flow in arteriovenous fistulas and grafts predisposes to LV volume overload.

13. Arteriosclerosis

Increased pulse pressure and Systolic Blood Pressure are closely correlated with LV hypertrophy[47, 48]. Raised pulse pressure[49, 51], increased carotid wall thickness[52] and elevated pulse wave velocity[53] have all been associated with an increased mortality. For any given systolic pressure, pulse pressure of more than 50 mm Hg correlates with increased risk of death.

14. Anemia-A Crucial Factor in the Vicious Cycle of Cardio renal Syndrome

The kidney being the main source of erythropoietin, anemia is apparently an integral part of advancing renal failure.

Low hemoglobin results in low oxygen delivery, reduced blood viscosity, reduced peripheral resistance leading to increased sympathetic activity and venous return. The resultant high cardiac output and high arterial volume lead to adaptive Left Ventricular Hypertrophy and arterial hypertrophy and defective cardiac remodeling.

Current guidelines define anemia as hemoglobin concentration less than 11 gm / dl in pre menopausal women and less than 12 gm / dl in males and post menopausal females.

In heart failure there is reduced blood pressure, increased sympathetic activity, and decreased renal blood flow. It induces cytokines which depress the bone marrow. The erythropoietin levels which should be 1000 times normal barely go up because of the inhibitory effect of TNF and renal disease.

The cytokines Tumor Necrosis Factor and interleukin-6 can decrease erythropoietin production in the kidney, increase erythropoietin

resistance in the bone marrow and decrease the release of iron from the reticuloendothelial system. TNF also interferes with the iron absorption in the gut.

Proteinuria itself causes loss of erythropoietin, iron, and transferrin, one reason why patients with nephrotic syndrome become anemic. In diabetics, glycosylation of the interstitial cells that produce erythropoietin lead to inappropriately low hemoglobin, the condition that is referred to as diabetic myocardiopathy in many cases, may simply be the anemia not treated adequately.

It is an independent risk factor for the development of electrocardiographically diagnosed LV hypertrophy[43] and of symptomatic heart failure[38]. In moderate to severe CKD before dialysis (GFR<50 ml/min), anemia is associated with LV growth. In dialysis patients, it is associated with progressive LV dilatation and hypertrophy[44] and with development of de novo heart failure[45].

For every 1gm/dl drop in mean hemoglobin, the risk of cardiac failure (de novo) increases by 25%, echocardiographically demonstrable LVH by 42% and risk of death increases by 14%.

Clinical Manifestations of cardiovascular system in CKD

1. LVH

Left Ventricular Hypertrophy is due to excessive pressure & volume loads. The principal factors comprising pressure & volume overload in patients with CKD are collectively known as hemodynamic risk factors.

Pressure overload results from sustained increases in LV after load that includes predominantly Hypertension, and Arteriosclerosis.

Volume overload embraces increased extra cellular volume, anemia and arteriovenous fistula.

Left Ventricular Hypertrophy can be concentric or eccentric[11] (asymmetrical). Concentric hypertrophy is considered an adaptive mechanism in response to chronic LV pressure over load. It is associated with increased thickness of both intra ventricular septum and LV free (or posterior) wall. The overall volume of ventricle remains normal, so that relative to the LV End diastolic diameter, wall thickness is increased.

Eccentric hypertrophy is a mechanism of adaptation to chronic volume over load in which LV end diastolic pressure tends to normalize at the expense of increased end diastolic volume.

Asymmetric hypertrophy is a variant of concentric hypertrophy whereby the septal wall is disproportionately thickened in relation to the LV posterior wall. This can result from an increase in after load, which exposes the septum to greater stress than free wall, or from stimulation of sympathetic nervous system.

2. Cardiac Failure

Functional Abnormalities

Assessment of LV functional abnormalities in patients with CKD is often difficult. Absence of symptoms does not imply intact functional reserve, regardless of the stage of the disease.

Diastolic dysfunction

CKD patients often have some impairment in LV diastolic function[12]. The abnormal ventricular filling in uremia results from increased LV stiffness caused by intramyocardial fibrosis and associated with delayed relaxation. By virtue of an increase in LV stiffness, small changes in volume results in large changes in LV pressure, predisposing to symptomatic pulmonary edema.

The reverse is also true: volume depletion results in large fall in LV pressure with symptomatic hypotension and hemodynamic instability.

This is often the presenting feature of diastolic dysfunction.

Systolic dysfunction

Resting systolic function is usually normal or increased in patients with advanced renal disease in the absence of antecedent cardiac disease[13-15].

Approximately 15% of patients have systolic dysfunction by the time they start dialysis. Diminished myocardial contractility may also be a result of overload cardiomyopathy, in which the myocardium relies on Starling forces to maintain a normal cardiac output.

This manifestation of cardiomyopathy has a substantially worse prognosis than that for either concentric hypertrophy or LV dilatation with normal systolic function.

3. Ischemic Heart Disease

In humans, basal myocardial perfusion tends to remain constant regardless of the severity of coronary artery stenosis.

During conditions requiring increased flow, a progressive relative decrease in perfusion occurs after the degree of stenosis is 40% or greater, and perfusion cannot increase above basal conditions when the stenosis is 80% or greater.

It appears that uremic milieu favor vascular wall damage.

Coronary Artery Disease, characterized by critical stenosis of major coronary arteries is highly prevalent in the CKD population.

Atheromatous ischemic heart disease in CKD is due to dyslipidemias, increased prothrombotic factors[16], increased oxidative stress that enhances atherogenesis[17], hyperhomocysteinemia[18, 19], disturbance of glucose metabolism[20]and cytokine activation.

Two factors have been suggested to play an important role in the formation of atheroma: Inflammation & Vascular calcification.

Evidence has shown that inflammation and C Reactive Protein (CRP) in general, contributes directly to atherosclerosis. CRP has been shown to bind to damaged cells, promoting activation of complement system. It displays calcium dependent binding and aggregation of Low Density Lipoproteins and Very Low Density Lipoproteins. It is a potent stimulator of tissue factor by monocytes.

Coronary atherosclerotic plaque morphology in patients with CKD was distinguished by abundant calcium deposition and such deposits may contribute substantially to high rate of complications in CKD.

3. Arrhythmias

They are due to disturbances in serum levels of electrolytes that can affect cardiac conduction including Potassium, Calcium, Magnesium[21, 22]. Old age, preexisting heart disease, LVH are associated with high prevalence of cardiac arrhythmias[23-25].

4. Valvular Heart Disease

Prevalence of aortic valve calcification in dialysis patients is 55%[26, 4] similar to that in elderly general population, although it occurs 10 to 20 years earlier[27-29].

Aortic valve stenosis in CKD evolves from valve sclerosis[7] .It may sometimes evolve rapidly to hemodynamically significant stenosis, with worsening of LVH and rapidly evolving symptomatology.

Age, increased phosphate level, increased Calcium Phosphorous product are the most important risk factor for development of aortic stenosis[26, 30]. Mitral valve annulus calcification is present in 15% of the patients[31]. Risk factors are involvement of posterior cusp, Left atrial dilatation, duration of pre-dialysis systolic hypertension[32].

Factors associated with decreased survival include severity of calcification, mitral regurgitation and decreased LV function.

5. Arteriosclerosis

It is defined as diffuse, non occlusive medial and intimal wall hypertrophy. It has been correlated with short stature, male gender, smoking, blood pressure, volume overload, humoral imbalance and age. The process of arteriosclerosis is accelerated in CKD patients. Arteriosclerosis leads to increased peripheral vascular resistance. Increased peripheral resistance is characterized principally by increased diastolic pressure and mean blood pressure. Whereas increased arterial stiffness is indicated by increased systolic blood pressure and widened pulse pressure. Increased systolic blood pressure and widened pulse pressure are closely correlated with LV hypertrophy.

6. Hypertension

It is due to increased extra cellular volume through salt and water retention, enhanced sympathetic activity, activation of Renin Angiotensin Aldosterone system and endothelial dysfunction[33-35].Additional factors include renal vasculopathy[36], hyperparathyroidism[37].

Electrocardiographic Changes in CKD[62]

The electrocardiographic changes in CKD are due to

1. LVH 2.Hypokalemia 3. Hyperkalemia 4. Hypocalcemia 5. Hypercalcemia 6. Pericarditis 7. Ischemic Changes 8. Pericardial Effusion

1. LVH

LV dilatation produces incomplete LBBB.

Romhilt Estes Scoring System For LVH

i) R or S in limb lead I $\geq$ 20 mm

Or S in lead V_1 or V_2

Or R in lead V_5 or$V_6 \geq$ 30 mm 3 points

ii) LV Strain

ST segment and T wave in opposite direction to QRS complex

Without Digitalis 3 points

With digitalis 1 point.

iii) Left Atrial Enlargement

Terminal negativity of P wave in lead $V_1 \geq 0.10$ mV in depth &

≥ 0.04 s in duration 3 points

iv) Left Axis deviation $\geq$ - 30degrees 2 points

v) QRS duration ≥ 0.09s 1 point

vi) Intrinsicoid deflection in lead $V_5 \geq 0.05$s 1 point

Total 15 points

LVH - 5 points

Probable LVH - 4 points

2. Hypokalemia

a) Flattening or inversion of T wave

b) Increased prominence of U wave

c) Slight depression of ST segment

d) Increased amplitude and width of P wave

e) Prolongation of PR interval

f) Premature beats and sustained tachyarrhythmias

g) Prolongation of QT_c interval

3. **Hyperkalemia**

   a) Increased amplitude and peaking of T wave

   b) Prolongation of PR interval

   c) Prolongation of QRS interval

   d) Flattening of P wave

   e) Disappearing ST segment

4. **Calcium Derangement**

   a) Hypocalcemia - prolonged QT_c interval

   b) Hypercalcemia - shortened QT_c interval

   $QT_c = QT/\sqrt{R\text{-}R}$

5. **Hypermagnesemia**

   It simulates Hyperkalemia.

   a) Widened QRS complex

   b) Prolongation of PR segment.

6. **Pericarditis**

   It is associated with 3 basic ECG abnormalities

Effect of acute pericardial injury

Acute pericarditis injures the epicardial surface of heart. This results in a shell of injured tissue, surrounding the heart, the brunt of which affects the apical segments. This is reflected by ST deviation towards the injured surfaces.

Effects on epicardial Ischemia

It is reflected by T wave inversion from the ischemic region.

i) Acute pericarditis

T wave change

During the very early phase of acute pericarditis, T wave usually becomes slightly taller, peaked and symmetrical. This may be the earliest sign.

ST segment changes

The epicardial injury is reflected as raised ST segment in leads oriented towards affected surface. Since there is no myocardial ischemia, T waves remain upright. The concavity in ST segment is facing upwards (saddle shaped).

Sub acute phase

ST segment tends to become convex upwards. The T wave loses its amplitude and becomes isoelectric. It eventually becomes inverted heralding the onset of chronic stage. ST also moves towards the base line.

ii) Chronic Pericarditis

T wave

Epicardial injury can progress to epicardial ischemia due to an associated myocarditis of epicardial layer. This results in widespread T wave inversion.

Low voltage complexes

This is due to short circuiting of electrical impulses by surrounding effusion.

Electrical Alternans

This manifest when there is substantial effusion, frequently seen in mid pre -cordial leads.

7. Pericardial Effusion

a) Low voltage complexes

b) Widespread ST segment elevation

c) It causes short circuiting of electrical impulse. This results in diminished magnitude of P, QRS and T wave as well as Total Electrical Alternans.

8. Ischemic Changes

a) Symmetric T wave inversion, b) ST segment flattening

c) Upwards sloping of ST segment depression,

d) Plane ST depression

Echocardiography

The term echocardiography refers to evaluation of cardiac structure and function with images and recordings produced by ultrasound. In the past three decades, it has rapidly become a fundamental component of cardiac evaluation. The development of echocardiography is credited to Elder and Hertz in 1954.

Types

1. M – mode Echo 2. Two dimensional Echo 3. Doppler Echo (continuous wave Doppler, pulsed wave Doppler, spectral Doppler) 4.Transesophageal Echo 5.Intravascular Ultrasonography 6. Fetal Echo 7. Three dimensional Echo

Advantages

1. **M – mode Echo** (M – motion)

Temporal resolution will be good. It can detect minimal pericardial effusion. It is used to obtain cardiac measurements.

2. **2-D Echo**

Spatial resolution will be good. Anatomical details of chambers, great vessels, valves can be studied in a better way.

3. **Doppler Echo**

It is used to detect stenosis or regurgitation and any shunt across inter atrial septum, inter ventricular septum, and for assessing diastolic function.

Continuous wave Doppler is used for quantification of valvular stenosis or regurgitation.

4. Trans esophageal Echo

It is helpful in assessing prosthetic valves, vegetations, aortic disease and intra cardiac masses.

It is used to monitor cardiac LV function throughout surgical procedure and into the post operative state.

Two Dimensional Echo

Two dimensional scanners utilize B-mode scan lines that are independently transmitted and received and are directed through a wedge shaped sector of cardiac anatomy by means of mechanical or electrical beam steering.

Standard 2D Echo cardio graphic transducer positions

Parasternal Position

Long axis

LV long axis

RV long axis

RV outflow

Short axis

Through the plane of

The cardiac base

The mitral valve

The chordae tendinae

The papillary muscles

The apex

Apical Position

Four chamber plane

Five chamber plane

Two chamber plane

Three chamber plane

Sub costal Position

Four chamber plane

Short axis through plane of

Mitral valve

Papillary muscle

Cardiac base

Suprasternal Position

Long axis (through ascending and descending aorta)

Short axis

Left parasternal position in long axis view provide excellent images of LV, Aorta, LA, mitral and aortic valves.

RV long axis view visualizes RA, RV and Tricuspid Valve.

In RV outflow view, Pulmonary Vein and Pulmonary Artery are seen.

The four chamber views are obtained from apical and sub costal positions.

Echocardiogram – Normal values

M – Mode measurements

LV function

i) LV end diastolic dimension (LVD)	3.7 - 5.6 cm
ii) LV end systolic dimension (LVS)	2.2 - 4.0 cm
iii) Inter ventricular septal thickness	0.6 - 1.2 cm

iv) LV posterior wall thickness	0.5 - 1.0 cm
v) Fractional Shortening	24 - 42%
vi) Ejection Fraction	55-60%

Mitral valve

i) MV EF slope	70 - 140 mm/sec
ii) MV DE amplitude	1.5 - 2.0 cm
iii) EPSS	0.9 cm

Aorta

i) Aortic Root diameter	2.0 - 3.7 cm
ii) Aortic valve opening	1.5 - 2.6 cm

Left Atrium

LA dimension	0.7 - 2.6 cm

Materials and Methods

The study was conducted in patients with CKD admitted in GRH, KMC during the period Jan – June 2007.

The following criteria were used in the selection of cases.

1. Patients with GFR of 30-59 ml/min

And/or

2. Patients with bilateral contracted kidneys on abdominal ultra sound with poor cortical medullary differentiation.

3. Patients with established CKD irrespective of etiology.

4. Patients with known Valvular Heart disease, Coronary artery disease, Systemic Hypertension on regular treatment & patients with poor pulmonary function were excluded.

In all patients, detailed history of illness was taken with special reference to cardiovascular symptoms and subjected to a complete clinical examination.

Blood biochemical investigations, ECG, Abdominal ultrasonography, complete hemogram were performed.

Echocardiography was done in all patients by a single echocardiographist to minimize observer variation.

GFR was calculated using Cockgraft-Gault Formula

In males

GFR = 1.2 × (140-age in years) × weight in kg / creatinine concentration in μ mol/L

In females the multiplying factor is 0.85 instead of 1.2.

Systolic function

In our study, systolic function is assessed mainly based upon M-mode measurements of LV function.

The ejection fraction is measured.

Normal range	55-80%
Mild systolic dysfunction	45-50%
Moderate systolic dysfunction	35-45%
Severe systolic dysfunction	<35 %

Diastolic function (Pulsed wave Doppler study)

Diastolic function is assessed by measuring mitral inflow, E/A measurements.

1. E/V-in m/s. it indicates initial mitral flow which causes ventricular filling following the opening of mitral valve.

2. A/V-in m/s. it indicates ventricular filling due to atrial systole.

3. E/A-is usually >1. E/A<1 indicates diastolic dysfunction.

Type I – Relaxation abnormality

Type II – Pseudo normalization

Type III – Restrictive abnormality

Regurgitation (color flow Doppler study)

Mitral regurgitation / tricuspid regurgitation

When regurgitation jet extends

Up to 1/3 of atrium : mild

1/2 of atrium : moderate

Posterior wall of atrium : severe

Aortic regurgitation

Jet height / LVOT height

Mild : ratio less than 20

Moderate : 20-40

Severe : more than 40

Pericardial effusion

Uremia produces chronic pericardial effusions. The pericardial fluid is hemorrhagic. Echocardiography is the procedure of choice for the diagnosis of pericardial effusion. The diagnostic feature on M mode echo is the persistence of an echo free space between parietal and visceral pericardium throughout the cardiac cycle. 2 D Echo has superior spatial orientation and allows delineation of size and distribution of pericardial effusion.

They are described as small, moderate and large based on the size of echo free space between the parietal and visceral pericardium on 2 D Echo.

Small : < 5 mm echo free space

Moderate : 5 – 10 mm

Large : > 10 mm

Fluid adjacent to the Right atrium is an early sign of pericardial effusion.

Observation and Analysis

Table 1

SEX	NO. OF PATIENTS	PERCENTAGE
Males	23	57.5%
Females	17	42.5%

In our study group that includes 40 patients, 57.5% of the affected patients were males.

Table 2

AGE IN YEARS	TOTAL		MALES		FEMALES	
	NO.	%	NO.	%	NO.	%
0-20	1	2.5%	-	-	1	2.5%
21-30	-	-	-	-	-	-
31-40	6	15%	3	7.5%	3	7.5%
41-50	14	35%	8	20%	6	15%
51-60	12	30%	6	15%	6	15%
> 60	7	17.5%	6	15%	1	2.5%

The age group most commonly affected is 41-50 years with male predominance.

Table 3

DURATION OF Ds IN MONTHS	TOTAL		MALE		FEMALES	
	NO	%	NO.	%	NO.	%
< 6	9	22.5%	6	15%	3	7.5%
7-12	10	25%	4	10%	6	15%
13-24	13	32.5%	9	22.5%	4	10%
25-36	4	10%	2	5%	2	5%
> 36	4	10%	2	5%	2	5%

In our study the average duration for cardiac disease to manifest in chronic kidney disease is 13-24 months.

Etiology	**No. of Cases**
i) Chronic Glomerulonephritis	7
ii) Hypertension	3
iii) Obstructive nephropathy	4
iv) Diabetic nephropathy	18
v) Chronic interstitial nephritis	6
vi) Autosomal dominant polycystic kidney ds	2

The commonest etiology in our study group is Diabetes Mellitus.

In this study, 38 patients have hemoglobin below 12gm% of which 10 patients have hemoglobin less than 8.0gm%.

Table 4

ECG Changes

SL. NO.	FINDING	NO. OF PATIENTS	MEAN
1.	LVH	25	62.5%
2.	LVC	6	15%
3.	ST-T Changes	12	30%
4.	LBBB	1	2.5%
5.	VPC	9	22.5%
6.	Ischemia	24	60%

The commonest ECG finding is Left Ventricular hypertrophy followed by ischemic changes.

Table 5

Chamber Dilatation

FINDING	NO. OF CASES	%
Dilated LV	9	22.5%
Concentric LVH	19	47.5%
All Chambers Dilated	5	12.5%
Dilated LA	7	17.5%

Concentric LVH is the most common echocardiographically detected abnormality in CKD patients.

Table 6

GRADING	MITRAL REGURGITATION	AORTIC REGURGITATION	TRICUSPID REGURGITATION
Trivial	4	3	1
Mild	7	4	4
Moderate	1	-	-

Aortosclerosis and posterior mitral annular calcification is present in about 35% of cases.

LV Function

Systolic Dysfunction

GRADING	NO. OF CASES	%
Mild	5	12.5%
Moderate	6	15%
Severe	-	-

Diastolic dysfunction

Type I – Diastolic dysfunction is present in about 50% of the cases.

LV Contraction

Global LV hypokinesia is present in two cases.

Pericardial Effusion

Pericardial effusion is present in 20% of cases.

DISCUSSION

Chronic renal failure is a constellation of signs and symptoms called uremia. It can present with features of involvement of any organ in the body. The present study is about cardiac involvement in CKD.

- Electrocardiogram showed evidence of LVH with or without strain pattern in 62.5% of cases.
- Low voltage complexes in 15% of cases.
- Occasional ventricular premature complexes in 22.5% of cases.
- Non-specific ST – T changes in 30% of cases.
- Electrocardiogram will reveal the presence of LVH and previous ischemic events.
- It is a sensitive index of cardiac effects of hyperkalemia.
- More accurate assessment of LV function and hypertrophy requires echocardiography.
- Regarding cardiac arrhythmias, their episodic nature makes identification and characterization difficult.
- Ideally 24 hours Holter monitoring, serial 12 lead ECG are necessary to detect ECG changes and cardiac arrhythmias in CKD patients.

- Gleason et al and Kimura et al[23-25] concluded that arrhythmias are due to acid base and electrolyte disturbances and underlying ischemic heart disease.
- Non sustained supraventricular tachyarrhythmias are common followed by ventricular premature complexes and ventricular tachycardia.

Echo revealed cardiac abnormalities in all cases.

Chamber dilatation

- 22.5% of Patients showed dilated LVH.
- 47.5% of Patients showed concentric LVH.
- In our study patients who have had long standing H/O Hypertension, show concentric LVH.
- The only major determinant of LVH in our study was the blood pressure burden.
- It correlates with the Harnett et al[62] study on impact of hypertension on cardiomyopathy, morbidity, mortality in ESRD.

- The concentric LVH includes Intra ventricular septal thickness in End Diastole. Anemia is an important determinant of End Diastolic Diameter.

- In our study the average Hemoglobin level was relatively 6-7gm%.[63-68]

- LA enlargement was not a frequent finding in our study. It is thought to be due to diastolic dysfunction due to LVH.

Valves

- Aortosclerosis and Posterior Mitral Annulus Calcification is found in 35% of patients in our study group.

- Age, duration and hyperparathyroidism have been cited as prime determinants of valvular calcification[26, 27].

- Myocardial fibrosis and cardiac calcification have been reported due to metastatic calcification.

LV Function

- Systolic dysfunction - 27.5% of cases

- Diastolic dysfunction - 50% of cases

- According to Kramer et al[12] factors contributing to development of CCF in patient with CKD are

  1. Volume over load 2. Valvular heart disease 3. Negative inotropic effects of Calcium 4. Cardiac arrhythmias 5. Pressure overload 6. Myocardial damage 7. Anemia.

- In our study, patients with moderate LV dysfunction showed features of volume overload, anemia and long standing history.

- All our patients revealed type I relaxation abnormality of diastolic dysfunction.

LV Contraction

- Global LV Hypokinesia reflects Dilated Cardiomyopathy.

Pericardial Effusion

- 20% of cases have pericardial effusion.

- Hemorrhagic pericardial effusion is a well recognized complication of uremia.

- In fact it can cause pericardial tamponade which is a life threatening emergency. Pericardial disease is an urgent indication for dialysis[69].

CONCLUSION

1. 41-50 year males were the most common affected people in our study group.

2. All patients were anemic.

3. The most common etiology was Diabetes.

4. LVH was the most common ECG finding noted.

5. Echo detection of cardiac changes was present in all patients.

6. Echocardiography is an invaluable tool in detecting early cardiac abnormalities in CKD. Hence Echo should be an integral part of assessment for renal transplant.

7. Cardiac changes were more frequent in those who were in advanced stages of chronic renal failure reflecting a positive correlation of cardiac changes with the severity of chronic renal failure.

8. Concentric LVH was the most common echocardiographically detected abnormality.

Diastolic dysfunction was present in 50% of cases and systolic dysfunction in 27.5% of cases.

PROFORMA

History

Name: **Age:** **Sex:**

Address:

Symptoms **Duration**

1. Oedema

2. Facial puffiness

3. Oliguria

4. Hematuria

5. Headache

6. Sleep disturbance

7. Convulsions

8. Weakness

9. Hemetemesis

10. Hiccough

11. Dyspnoea

12. Chest pain

13. Amenorrhoea

H/O Antecedent illness

Hypertension	Calculi	UTI
Diabetes	AGE	Sore throat
Tuberculosis	Transfusion	Scabies
Drugs	Proteinuria	
Jaundice	Hematuria	

Personal History

Smoking	Analgesics
Alcohol	Indigenous medicines

Obstetric History

No. of Pregnancies / Abortion

Hypertension / Edema / Proteinuria

Family History

Diabetes, Hypertension, Tuberculosis, Hematuria

Renal disease, Deafness, Visual disturbance

EXAMINATION

General Examination

Height	Pulse	Anemia	Skin
Weight	BP	Jaundice	Nails
Build	Temperature	Edema	Teeth
Face		Lymph node	Eyes

CVS

JVP	Heart sounds
Precordium	Murmur
Apex beat	Pericardial rub

RS

Trachea	Breath sounds
Chest movements	Adventitious sounds
Percussion	

Abdomen

Appearance	Liver	Kidney
Free fluid	Spleen	Bruit

CNS

Higher functions	cranial nerves	Spinomotor system
Sensory system	Fundus	

Miscellaneous

Bones / joints	Genitalia
P / R	P / V

Lab Data

Urine	**CBC**	**Blood Bio-chemistry**	
Albumin	Hb	Urea	HCO3
Sugar	Tc	Creatinine	Na
Deposits	Dc	Protein	K
Pr / Cr	PCV	A / G	Ca,P

X – Ray

1. CXR 2. KUB – Abdomen

USG

Kidney size	Cortical medullary differentiation

ECG

Rate	Rhythm	PR interval	Axis
ST - T changes	U waves	Chamber hypertrophy	

Echocardiography

LVd	LVs	EF
Valves	Chambers	Pericardium

Master chart

S.NO	Name	Age	Sex	Duration (months)	Pulse	BP	Pallor	Edema	Oliguria	JVP	CVS S1S2	Murmur	Rs Crepts	Abdomen Ascites	Abdomen Liver	CNS CVA	USG LK	USG RK
1.	Anjalai	45	F	12	98	150/90	+	+	+	↑	+	-	+	-	+	-	10×4.2	10.1×4.1
2.	Kasiammal	43	F	8	84	160/100	+	-	-	-	+	-	-	-	-	-	6.2×2.6	6.1×2.5
3.	Krishnan	55	M	24	90	170/90	+	+	+	-	+	-	+	-	-	-	7.2×2.1	7.4×2.6
4.	Rajaiah	60	M	15	84	160/100	+	-	-	-	+	-	+	-	-	-	7.2×3.8	7.4×4
5.	Sankar	35	M	19	84	180/90	+	-	-	-	+	-	-	-	-	-	6.9×3.9	7.5×3.6
6.	Jagaraman	60	M	6	84	160/90	+	+	+	-	+	-	-	-	-	-	8.7×3.2	8.7×3.1
7.	Rathnasabapathy	65	M	13	84	150/90	+	-	+	-	+	-	-	-	-	-	8.2×4.2	8.7×4.9
8.	Thirupathy	40	M	8	84	150/90	+	+	+	-	+	-	-	-	-	-	8.9×1.5	8.7×3
9.	Rangaraju	50	F	14	90	140/90	+	+	-	-	+	-	-	-	-	-	6.6×3.2	7.9×3.7
10.	Sumeela	60	F	16	88	170/100	+	-	-	-	+	-	-	-	-	-	8.8×4.1	8.6×2.5
11.	Babajan	60	M	18	80	170/100	+	+	-	-	+	-	-	-	-	-	6-2×2.8	6×3.6
12.	Jayamma	65	F	20	98	150/100	+	-	-	-	+	-	-	-	-	-	6.2×1.8	7.4×3.2
13.	Pothalanathy	64	M	4	88	160/90	+	-	-	-	+	-	-	-	-	-	8.7×5.1	10.1×3.2
14.	Baby	58	F	14	86	200/100	+	+	+	↑	S3+	-	+	-	-	-	8.8×3.1	8.2×3.1
15.	Jagannathan	45	M	15	88	200/100	+	+	-	-	+	-	+	-	-	-	9.3×3.1	8.7×3.7
16.	Murugavel	34	M	36	78	180/100	+	+	+	-	+	-	+	-	+	-	4.8×2.6	6.3×2.2
17.	Dhanasekar	34	M	36	90	140/100	+	-	-	-	+	-	+	-	-	-	8.7×1.5	8.4×2.2

S.NO	Name	Age	Sex	Blood		Urine		Blood Biochemistry								ECG					
				HG	TC	Alb	Sug	Sug	Urea	Creat	SAP	S.Pr	Na^+	K^+	CXR	LVH	ST-T	LVC	VPC	LBBB	Ischemia
1.	Anjalai	45	F	9.0	8000	++	nil	180	84	6.8	32	5.5	130	5.2	CTR↑	–	–	–	+	–	HL
2.	Kasiammal	43	F	4.2g%	7200	trace	–	130	51	5.7	40	5.7	132	4.8	(N)	–	+	–	–	–	–
3.	Krishnan	55	m	8.0	9800	–	–	120	95	5.8	34	6.8	140	5.4	CTR↑	–	+	–	+	–	IN
4.	Rajaiah	60	m	8.0	15,000	++	–	176	94	6.5	36	6.5	134	5.0	CTR↑	–	+	–	–	–	AW
5.	Sankar	35	M	7.0	8000	++	–	98	84	6.5	38	4.8	140	4.6	"	+	–	+	–	–	IL
6.	Jayaraman	60	m	7.8	5700	++	–	170	52	6.0	33	5.3	140	3.8	"	+	–	+	–	–	AW
7.	Rathnaswapathy	65	m	8.5	7500	++	–	120	65	5.5	42	6.4	130	3.5	(N)	–	–	–	–	–	IL
8.	Thirupathy	40	m	8.6	8400	++	–	102	98	12.0	40	6.5	124	5.4	CTR↑	+	–	–	–	–	HL
9.	Ranganayaki	50	F	9.0	7400	+	–	138	88	6.0	32	6.0	120	3.2	"	+	–	+	–	–	IL
10.	Susecla	60	F	9.2	9200	+	–	120	86	7.0	34	6.8	135	4.2	(N)	–	+	–	–	–	–
11.	Babajoo	60	m	9.1	5300	+	–	110	68	5.8	31	5.2	134	4.3	CTR↑	+	–	–	+	+	HL
12.	Jayamma	65	F	6.8	9400	+	–	128	48	5.5	35	5.5	135	3.6	(N)	(+)	–	–	–	–	IN
13.	Panthavarathy	64	m	8.6	5700	++	–	134	68	5.3	36	5.7	132	4.8	(N)	+	–	–	–	–	–
14.	Baby	58	F	5.8	7000	++	–	136	60	8.3	37	7.0	128	4.5	CTR↑	–	+	–	+	–	–
15.	Jagannatham	45	m	9.7	8200	+	–	138	67	5.3	36	6.8	138	2.8	"	+	–	–	–	–	AS
16.	Murugavel	34	m	8.0	7800	trace	–	140	86	5.2	39	5.6	126	3.0	"	+	–	–	–	–	IN
17.	Dharasekar	34	m	14.2	8000	++	–	134	69	7.0	34	5.9	143	3.4	"	+	–				

S.NO	Name	Age	Sex	Duration months	pulse	BP	Pallor	edema	oliguria	JVP	CVS S_1S_2	CVS Pericardial rub	Rs crepts	Rs Pleural effusion	Abdomen Ascites	Abdomen FF	CNS Asterixis	CVA	USG RK	USG LK
18.	Periyasamy	52	m	48	86	130/80	+	+	+	↑	+	−	+	−	−	+	−	−	8.7×4.9	10×4.5
19.	Arumugam	55	m	4	90	130/90	+	+	+	−	+	−	−	−	+	−	−	−	9.0×4.3	8.8×4.4
20.	Dhanalaxmi	46	F	24	80	220/100	+	+	−	−	+	−	−	−	−	−	−	−	8.8×3.6	8.9×4.6
21.	Varalaxmi	36	F	4	84	130/80	+	+	−	−	+	−	+	−	−	−	−	−	7.2×3.1	8.1×3.1
22.	Kabali	55	m	12	90	230/120	+	+	−	−	+	−	−	−	−	−	−	−	8.0×3.1	7.9×2.5
23.	Chinnaiah	42	m	48	88	170/100	+	−	−	−	+	−	−	−	−	−	−	−	7×3.3	7.1×3.2
24.	Raman	65	M	14	84	150/90	+	+	−	−	+	−	+	−	−	−	−	−	8×4.0	8.1×4.2
25.	Sathyapriya	16	F	12	88	170/120	+	+	−	−	+	−	−	−	−	−	−	−	7×2.8	Absent
26.	Adhilaxmi	53	F	12	80	140/90	+	−	−	−	+	−	−	−	−	−	−	−	7.9×3.8	7.8×4.2
27.	Kabali	50	m	4	84	220/110	+	−	−	−	+	−	−	−	−	−	−	−	8.6×3.1	7.9×2.5
28.	Somasundar	65	m	4	84	150/90	+	+	−	−	+	−	+	−	−	−	−	−	6.4×2.9	7.7×3.9
29.	Nagammal	50	F	5	89	140/90	+	−	−	−	+	−	−	−	−	−	−	−	8.8×2.3	7.9×3.4
30.	Sagunthala	53	F	36	90	140/50	+	−	−	−	+	−	−	−	−	−	−	−	6.4×2.8	6.1×3.1
31.	Dharmalingam	45	m	24	90	130/90	+	+	−	−	+	−	−	−	−	−	−	−	8.4×4.2	8.8×4.8
32.	Rajesh	45	m	12	84	140/100	+	−	−	−	+	−	−	−	−	−	−	−	11.8×4.5 Σ cysts	11.5×4.5 cysts+
33.	Lakshmi	60	F	12	80	170/110	+	+	−	−	+	−	+	−	−	−	−	−	7.7×2.1	7.2×2.7
34.	Polaiah	50	m	5	80	150/90	+	−	−	−	+	−	−	−	−	−	−	−	7.5×2.8	7.8×3.8
35.	Raju	48	m	24	84	150/90	+	+	−	−	+	−	−	−	−	−	−	−	10.2×4.8 cysts+	10.2×3.5 cysts+
36.	Kalairani	35	F	20	90	200/140	+	−	−	−	+	−	+	−	−	−	−	−	6×2.4	6.5×3.0

S.NO	Name	Age	Sex	Blood		Urine		Blood biochemistry							CXR	ECG					Ischemia
				Hb	Tc	Alb	Sug	Sug	Urea	Creat	SAP	SPr	Na^+	K^+		LVH	ST-T	LVC	VPC	LBBB	
18.	Periyasamy	52	m	9.0	7400	+++	–	98	63	5.3	48	5.6	137	4.5	CTR↑	+	–	+	–	–	HL
19.	Arumugam	55	m	9.6	7800	+	–	120	91	8.5	36	4.5	130	5.4	"	–	–	–	–	–	IW
20.	Dhanalaxmi	46	F	8.5	10,600	–	–	130	48	5.8	33	6.5	135	5.2	"	+	–	–	–	–	IW
21	Varalaxmi	36	F	8.6	7000	++	–	128	82	7.0	31	5.5	130	3.8	"	+	–	+	–	–	Global
22.	Kabali	55	m	8.2	6200	–	–	130	88	6.6	30	5.6	136	4.8	(N)	+	–	–	–	—	–
23.	Chinnaiah	42	m	9.1	5000	+	–	124	87	5.0	43	6.8	123	3.2	"	+	–	–	–	–	HL
24.	Ramar	65	m	6.6	8200	–	–	128	34	10.9	41	7.2	126	5.0	CTR↑	+	–	–	–	–	Global
25.	Sathyapriya	16	F	8.3	6500	–	–	136	112	9.8	39	5.3	130	3.8	"	+	–	–	–	–	–
26.	Adhilaxmi	53	F	9.9	5600	+	–	134	121	6.7	38	5.4	130	4.2	(N)	–	+	–	–	–	–
27.	Kabali	50	m	9.4	6200	+	–	128	88	6.0	43	6.4	136	4.8	CTR↑	+	–	–	–	–	–
28	Somasundar	65	m	7.9	4700	+	–	130	82	6.8	45	6.1	152	5.5	"	+	–	–	+	–	–
29.	Nagammal	50	F	6.5	4800	–	–	128	90	5.5	46	6.0	138	4.9	(N)	–	+	–	+	–	HL
30.	Sagunthala	53	F	6.6	7600	+	–	124	87	5.4	47	4.3	130	3.8	(N)	–	–	–	+	–	AL
31.	Dharmalingam	45	m	9.1	7400	+++	–	128	48	5.1	43	3.1	135	4.3	(N)	+	–	–	–	–	—
32	Rajesh	45	m	14.2	7800	–	–	130	50	5.5	40	6.8	135	4.3	"	–	+	–	+	–	–
33.	Lakshmi	60	F	8.4	6700	–	–	140	47	6.1	31	5.7	133	4.8	CTR↑	–	+	+	–	–	–
34	Polaiah	50	m	9.0	6800	+	–	138	48	6.0	35	5.6	134	4.9	(N)	+	+	–	–	–	†
35	Raju	48	m	8.6	5600	trace	–	126	34	5.8	39	5.4	133	5.0	"	+	–	–	–	–	AL
36.	Kalaivani	35	F	9.0	8200	"	–	110	52	12.0	44	5.8	131	5.1	CTR↑	+	–	–	–	–	—

S.NO	Name	Age	Sex	Pulse rate	Pulse	BP	Pallor	edema	oliguria	JVP	CVS		RS		Abdomen		CNS		USG	
											S_1S_2	Perub	crepts	Plrub	org	FF	Asterixis	CVA	LK	RK
37.	Ayesha	55	F	4	90	160/90	+	-	+	-	+	-	-	-	-	-	-	-	6×3·3	6×3·1
38.	Bujjaiah	60	m	12	88	140/80	+	-	-	-	+	-	-	-	+	-	-	-	10×3·1 cysts +	10×4·8 cysts +
39.	Renuka	33	F	8	82	120/100	+	-	-	-	+	-	-	-	-	-	-	-	8·8×4·2	8·7×4·1
40.	Kamamma	45	F	36	84	180/100	+	-	-	-	+	-	-	-	-	-	-	-	6·7×2·2	6·6×2·3

S.NO	Name	Age	Sex	Blood		Urine			Blood Biochemistry							ECG				
				Hb	Tc	alb	Sug	Sug	Urea	Creat	SAP	SPr	Na^+	K^+	CR	LVH	ST-T	LVC	VPC	LBBB	Ischemia
37.	Ayesha	55	F	8·6	6200	trace	~~138~~	138	48	6·2	43	5·1	133	4·8	(N)	-	+	-	-	-	-
38.	Bujjaiah	60	m	5·8	7100	++	-	128	50	7·1	49	5·8	134	5·1	CTR↑	+	-	-	-	-	Global
39.	Renuka	33	F	9·8	8000	+++	-	136	45	5·1	38	4·5	136	4·8	(N)	-	+	-	-	-	-
40.	Kamamma	45	F	8·8	7200	+	-	144	83	5·0	31	5·9	137	4·9	(N)	+	-	-	+	-	AL

Echo

S.NO	Name	LVD	LVS	LA	EF	LVH	Calcified valve	Regurgit	PE	DD
1.	Anjalai	4.5	2.8	0.8	40%	–	+	+	–	–
2.	Kasiammal	4.8	2.7	0.7	48%	+	+	–	–	–
3.	Krishnan	4.8	3.3	0.7	58%	+	+	+	–	+
4.	Rajaiah	4.6	2.7	0.8	49%	+	–	+	–	+
5.	Sankar	5.9	4.1	2.7	57%	+	–	–	+	–
6.	Jayaraman	4.6	3.0	0.8	60%	+	–	–	+	+
7.	Rathasabapathy	5.0	3.3	0.8	58%	–	+	+	–	–
8.	Thirupathy	5.4	3.3	0.9	68%	+	–	+	–	+
9.	Ranganayaki	6.6	5.3	2.9	38%	–	–	+	+	–
10.	Suseela	4.8	3.1	0.8	64%	–	–	–	+	+
11.	Babajon	6.5	4.7	2.9	40%	–	+	+	–	–
12.	Jayamma	5.6	3.8	3.0	60%	+	+	+	–	–
13.	Parthasarathy	5.4	3.7	2.6	60%	+	+	–	–	+
14.	Baby	4.8	3.1	2.5	48%	+	–	+	–	–
15.	Jeganathan	5.3	4.3	3.6	37%	+	–	+	–	–
16.	Murugavel	5.3	3.6	2.5	56	–	–	+	+	+
17.	Dhanasekaran	4.9	2.8	2.3	74	+	–	–	–	+
18.	Periyasamy	5.9	4.9	2.3	44	+	–	+	+	–
19.	Arumugam	4.2	3.8	2.1	67	–	+	–	–	–
20.	Dhanalaxmi	5.1	3.2	2.1	68	+	+	+	–	–
21.	Kanalaxmi	5.2	4.2	2.9	50	–	–	–	+	–

S.NO	Name	LVD	LVS	LA	EF	LVH	Calcified valve	Regurgitation	PE	DD
22.	Kabali	4.7	2.7	0.9	76	+	–	+	–	–
23.	Chinnaiah	5.1	3.4	1.2	63	+	+	+	–	+
24.	Raman	5.9	3.3	3.0	88	+	–	–	–	–
25.	Sathyapriya	5.8	3.6	2.3	58	–	–	+	–	–
26.	Adhilaxmi	3.9	2.4	0.9	70	–	+	+	–	+
27.	Kalali	5.8	3.6	1.1	76	+	–	+	–	–
28.	Somasundri	4.6	3.6	1.2	58	+	+	+	–	–
29.	Nagamma	4.5	2.9	1.0	64	–	+	–	–	+
30.	Sagunthala	3.6	2.4	1.4	65	–	–	–	–	+
31.	Dharma-lingam	5.5	3.6	1.3	64	–	–	–	–	+
32.	Rajesh	4.6	2.6	1.2	75	–	–	–	+	+
33.	Lakshmi	4.9	2.8	1.3	73	–	–	–	–	+
34.	Polaiah	5.8	3.9	1.3	58	–	–	+	–	–
35.	Raju	5.2	3.5	1.2	70	–	–	+	–	+
36.	Kalaivani	5.1	3.6	1.4	46	–	+	+	–	+
37.	Ayesha	4.8	3.0	1.5	68	–	+	+	–	–
38.	Brijjaiah	5.9	4.9	2.8	42	–	+	+	–	+
39.	Renuka	4.2	3.7	0.9	70	–	+	+	–	+
40.	Kamsunisa	3.7	2.4	0.8	67	+	–	–	–	+

BIBLIOGRAPHY

1) O'Neill WC: Sonographic evaluation of renal failure. Review. Am J Kidney Dis 35:1021-1038, 2000.

2) Oxford Text book of medicine- fourth edition- 2003

3) K/DOQI Clinical Practice Guidelines for Chronic Kidney Disease: Evaluation, classification, and stratification. Kidney Disease Outcome Quality Initiative. Am J Kidney Dis 2002 39:S1-S246, 2002.

4) London GM, Pannier B, Guerin AP, et al: Cardiac hypertrophy, aortic compliance, peripheral resistance, and wave reflection in end-stage renal disease: Comparative effects of ACE inhibition and calcium channel blockade. Circulation 90:2786-2796, 1994.

5) Mazzaferro S, Coen G, Bandini S, et al: Role of ageing, chronic renal failure and dialysis in the calcification of the mitral annulus. Abstract. Nephrol Dial Transplant 8:335-340, 1993.

6) London GM, Pannier B Marchais SJ, Guerin AP: Calcification of the aortic valve in the dialyzed patient. J Am Soc Nephrol 11:778-783, 2000.

7) Otto CM. Lind BK. Kitzman DW, et al: Association of aortic-valve sclerosis with cardiovascular mortality and morbidity in the elderly. N Engl J Med 341:142-147, 1999.

8) Levin A, Singer J, Thompson CR, et al: Prevalent left ventricular hypertrophy in the pre dialysis population: Identifying opportunities for intervention. Am J Kidney Dis 27:347-354, 1996.

9) Barrett BJ, Parfrey PS, Morgan J, et al: Prediction of early death in end-stage renal disease patients starting dialysis. Am J Kidney Dis 29:214-222, 1997.

10) Levin A, Thompson CR, Ethier J, et al: Left ventricular mass index increase in early renal disease: Impact of decline in hemoglobin. Am J Kidney Dis 34:125-134, 1999.

11) Hunter JJ, Chien KR: Signaling pathways for cardiac hypertrophy and failure. N Engl J Med 341:1276-1283, 1999.

12) Kramer W, Wizemann V, Lammlein G, et al: Cardiac dysfunction in patients on maintenance hemodialysis: II: Systolic and diastolic properties of the left ventricle assessed by invasive methods. Contrib Nephrol 52:97-109, 1986.

13) Verbeelen D, Bossuyt A, Smitz J, et al: Hemodynamics of patients with renal failure treated with recombinant human erythropoietin. Clin Nephrol 31:6-11, 1989.

14) Cannella G, La Canna G, Sandrini M, et al: Renormalization of high cardiac output and of left ventricular size following long-term recombinant human erythropoietin treatment of anemic dialyzed uremic patients. Clin Nephrol 34:272-278, 1990.

15) McMahon LP, Mason K, Skinner SL, et al: Effects of haemoglobin normalization on quality of life and cardiovascular parameters in end-stage renal failure. Nephrol Dial Transplant 15:1425-1430, 2000.

16) Culleton BF, Wilson PWF: Thrombogenic risk factors for cardiovascular disease in dialysis patients. Semin Dial 12:117-125, 1999.

17) Khaper N, Rigatto C, Seneviratne C, et al: Chronic treatment with propranolol induces antioxidant changes and protects against ischemia-reperfusion injury. J Mol Cell Cardiol 29:3335-3344, 1997.

18) Bostom AG, Lathrop L: Hyperhomocysteinemia in end-stage renal disease: Prevalence, etiology, and potential relationship to arteriosclerotic outcomes. Kidney Int 52:10-20, 1997.

19) Friedman AN, Bostom AG, Selhub J, et al: The Kidney and homocysteine metabolism. J Am Soc Nephrol 12:2181-2189, 2001.

20) London GM, Drueke TB: Atherosclerosis and arteriosclerosis in chronic renal failure. Kidney Int 51:1678-1695, 1997.

21) D'Elia JA, Weinrauch LA, Gleason RE, et al: Application of the ambulatory 24-hour electrocardiogram in the prediction of cardiac death in dialysis patients. Arch Intern Med 148:2381-2385, 1988.

22) Blumberg A, Hausermann M, Strub B, Jenzer HR: Cardiac arrhythmias in patients on maintenance hemodialysis. Nephron 33:91-95, 1983.

23) Kimura K, Tabei K, Asano J, Hosoda S: Cardiac arrhythmias in hemodialysis patients: A study of incidence and contributory factors. Nephron 53:201-207, 1989.

24) Wizemann V, Kramer W, Thormann J, et al: Cardiac arrhythmias in patients on maintenance hemodialysis: Causes and management. Contrib Nephrol 52:42-53, 1986.

25) Gruppo Emodialisi e Pathologia Cardiovasculari: Multicentre cross-sectional study of ventricular arrhythmias in chronically hemodialysed patients. Lancet 6:305-309, 1988.

26) Ribeiro S, Ramos A, Brandao A, et al: Cardiac valve calcification in haemodialysis patients: Role of calcium-phosphate metabolism. Nephrol Dial Transplant 13:2037-2040, 1998.

27) Maher ER, Young G. Smyth-Walsh B. et al: Aortic and mitral valve calcification in patients with end-stage renal disease. Lancet 2:875-877, 1987.

28) Braun J, Oldendorf M, Moshage W, et al: Electron beam computed tomography in the evaluation of cardiac calcification in chronic dialysis patients. Am J Kidney Dis 27:394-401, 1996.

29) Urena P. Malergue MC. Goldfarb B. et al: Evolutive aortic stenosis in hemodialysis patients: Analysis of risk factors. Nephrologie 20:217-225, 1999.

30) Rosenhek R. Binder T. Porenta G. et al: Predictors of outcome in severe, asymptomatic aortic stenosis. N Engl J Med 343:611-617, 2000.

31) Fernandez-Reyes MJ, Auxiliadora Bajo M, Robles P, et al: Mitral annular calcification in CAPD patients with a low degree of hyperparathyroidism: An analysis of other possible risk factors. Nephrol Dial Transplant 10:2090-2095, 1995.

32) Huting J: Predictive value of mitral and aortic valve sclerosis for survival in end-stage renal disease on continuous ambulatory peritoneal dialysis. Nephron 64:63-68. 1993.

33) Xiao S, Schmidt RJ, Baylis C: Plasma from ESRD patients inhibits nitric oxide synthase activity in cultured human and bovine endothelial cells. Acta Physiol Scand 168:175-179, 2000.

34) Schroder M, Riedel E, Beck W, et al: Increased reduction of dimethylarginines and lowered inter dialytic blood pressure by the use of biocompatible membranes. Kid Int Suppl 78:S19-S24, 2001.

35) Surdacki A, Sulowicz W, Wieczorek-Surdacka E, Herman ZS: Effect of a hemodialysis session on plasma levels of endothelin-1 in hypertensive and normotensive subjects with end-stage renal failure. Nephron 81:31-36, 1999.

36) Schieppati A, Remuzzi G: Prevalence and significance of hypertension in systemic lupus erythematosus. Am J Kidney Dis 21(5 suppl 2): 58-60, 1993.

37) Raine AE, Bedford L, Simpson AW, et al: Hyperparathyroidism, platelet intracellular free calcium and hypertension in chronic renal failure. Kidney Int 43:700-705, 1993.

38) Rigatto C, Foley RN, Kent GM, et al: Long-term changes in left ventricular hypertrophy after renal transplantation. Transplantation 70:570-575, 2000.

39) Sarnak MJ, Coronado BE, Greene T, et al: Cardiovascular disease risk factors in chronic renal insufficiency. Clin Nephrol 57:327-335, 2002.

40) Kasiske BL: Hyperlipidemia in patents with chronic renal disease, Am J Kidney Dis 32 (5 supple 3): S142 – S156, 1998.

41) Levin A, Djurdjev O, Barett B, et al: Cardiovascular disease in patients with chronic kidney disease: Getting to the heart of the matter. Am J Kidney Dis 38:1398-1407, 2001.

42) Grossman E, Shemesh E, Shamiss A, et al: Left ventricular mass in diabetes-hypertension. Arch Intern Med 152:1001-1004, 1992.

43) Rigatto C, Foley RN, Jeffrey J, et al: Electrocardiographic left ventricular hypertrophy in renal transplant recipients: Prognostic value and impact of blood pressure and anemia. J Am Soc Nephrol 14:462-468, 2003.

44) 398-1407, Foley RN, Parfrey PS, Kent GM, et al: Long-term evolution of cardiomyopathy in dialysis patients. Kidney Int 54:1720-1725, 1998.

45) Harnett JD, Foley RN, Kent GM, et al: Congestive heart failure in dialysis patients: Prevalence, incidence, prognosis, and risk factors. Kidney Int 47:884-890, 1995.

46) Enia G, Mallamaci F, Benedetto FA, et al: Long-term CAPD patients are volume expanded and display more severe left ventricular hypertrophy than haemodialysis patients. Nephrol Dial Transplant 16:1459-1464, 2001.

47) Greaves SC, Gamble GD, Collins JF, et al: Determinants of left ventricular hypertrophy and systolic dysfunction in chronic renal failure. Am J Kidney Dis 24:768-776, 1994.

48) Blacher J, Guerin AP, Pannier B, et al: Impact of aortic stiffness on survival in end-stage renal disease. Circulation 99:2434-2439, 1999.

49) Guerin AP, Blacher J, Pannier B, et al: Impact of aortic stiffness attenuation on survival of patients in end-stage renal failure. Circulation 103:987-992, 2001.

50) Tozawa M, Iseki K, Iseki C, Takishita S: Pulse pressure and risk of total mortality and cardiovascular events in patients on chronic hemodialysis. Kidney Int 61:717-726, 2002.

51) Klassen PS, Lowrie EG, Reddan DN, et al: Association between pulse pressure and mortality in patients undergoing maintenance hemodialysis. JAMA 287:1548-1555, 2002.

52) Benedetto FA, Mallamaci F, Tripepi G, Zoccali C: Prognostic value of ultrasonographic measurement of carotid intima media thickness in dialysis patients. J AM Soc Nephrol 12:2458-2564, 2001.

53) Nishikimi T, Minami J, Tamano K, et al: Left ventricular mass relates to average systolic blood pressure, but not loss of circadian blood pressure in stable hemodialysis patients: An ambulatory 48-hour blood pressure study. Hypertens Res Clin Exp 24:507-514, 2001.

54) Foley RN, Parfrey PS, Harnett JD, et al: Hypoalbuminemia, cardiac morbidity, and mortality in end-stage renal disease. J Am Soc Nephrol 7:728-736, 1996.

55) Bostom AG, Silbershatz H, Rosenberg lH, et al: Non fasting plasma total homocysteine levels and all-cause and cardiovascular disease mortality in elderly Framingham men and women. Arch Intern Med 159:1077-1080, 1999.

56) Kark JD, Selhub J, Adler B, et al: Non fasting plasma total homocysteine level and mortality in middle-aged and elderly men and women in Jerusalem. Arch Intern Med 131:321-330, 1999.

57) Boston AG, Shemin D, Verhoef P, et al: Elevated fasting total plasma homocysteine levels and cardiovascular disease outcomes in maintenance dialysis patients: A prospective study. Arterioscl Thromb Vasc Biol 17:2554-2558, 1997.

58) Suliman ME, Qureshi AR, Barany P, et al: Hyperhomocysteinemia, nutritional status, and cardiovascular disease in hemodiaylsis patients. Kidney Int 57:1727-1735, 2000.

59) . Tetta C, Biasioli S, Schiavon R, et al: An overview of haemodialysis and oxidant stress. Blood Purif 17:118-126, 1999.

60) Becker BN, Himmelfarb J, Henrich WL, Hakim RM: Reassessing the cardiac risk profile in chronic hemodialysis patients: A hypothesis on the role of oxidant stress and other non-traditional cardiac risk factors. J Am Soc Nephrol 8:475-486, 1997.

61) Rostand SG, Drueke TB: parathyroid hormone, vitamin D, and cardiovascular disease in chronic failure. Kidney Int 56: 383-392, 1999.

62) Marriott's practical ECG – 10th Edition

63) Foley RN, Parfrey PS, Harnett JD, et al: Impact of hypertension on cardiomyopathy, morbidity and mortality in end-stage renal disease. Kidney Int 49:1379-1385, 1996.

64) Levin A: Anemia and left ventricular hypertrophy in chronic kidney disease populations: A review of the current state of knowledge. Kidney Int Suppl (80):35-38, 2002.

65) Levin A: The role of anemia in the genesis of cardiac abnormalities in patients with chronic kidney disease. Nephrol Dial Transplant 17:207-210, 2002.

66) Levin A, Thompson CR, Ethier J, et al: Left ventricular mass index increase in early renal disease. Impact of decline in hemoglobin. Am J Kidney Dis 34:125-134, 1999.

67) Levin A: Anemia in the patient with renal insufficiency: Documenting the impact and reviewing treatment strategies. Nephrol Dial Transplant 14:292-295, 1999.

68) Levin A, Djurdjev O, Barrett B, et al: Cardiovascular disease in patients with chronic kidney disease: Getting to the heart of the matter. Am J Kidney Dis 38:1 2001.

69) Baldwin J.J, Edwards J.E, et al : Uremic Pericarditis as cause of Tamponade. Circulation 53, 896 – 901.